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# BORDEN'S REVIEW

# *of*

# NUTRITION RESEARCH

## NUTRITION AND ALCOHOLISM

### *The Genetotrophic Approach*

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# NUTRITION RESEARCH

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# NUTRITION AND ALCOHOLISM

## *The Genetotrophic Approach*

By RUTH WOODS

That individuals are different in their nutritional wants and requirements is obvious to everyone. The nursery rhyme that Jack Sprat could eat no fat and his wife could eat no lean is a statement of this obvious fact. Yet in the development of the science of nutrition, attention has been focused more upon the requirements common to different people rather than to individual differences. This was more or less inevitable. In the development of any science oversimplification and overgeneralization are the rule. With increasing maturity and sophistication, small differences which would have been cast aside earlier as experimental errors or as inconsistent with a to-be proved theory are looked upon with increasing interest and new insight.

In nutrition and biochemistry the differences between individuals have been recognized for many years. However, only a few isolated investigations have been carried out to determine the causes of such differences. One of the most important of these was the work of Garrod whose classic "Inborn Errors of Metabolism," stressed the hereditary origin of biochemical differences among individuals. That physical or structural differences are hereditary is well known. Red hair runs in families; blue-eyed parents have blue-eyed children. Garrod's contribution was that biochemical attributes are just as subject to the laws of Mendelian heredity and genetics as are the more apparent structural characteristics.

Following Garrod's work a few brilliant researchers in the new field of biochemical genetics kept the field alive, but it has only been in the last ten or fifteen years that this field has come into its own as a powerful tool making possible new approaches to many otherwise intractable problems of biochemistry and nutrition.

This subject will be discussed in more detail in a future issue of *Borden's Review of Nutrition Research.* The present review will discuss one of the most significant and promising applications of research in individual biochemistry as opposed to species biochemistry: The concept of *genetotrophic disease,* a disease of nutritional deficiency resulting from inherited peculiarities in the chemistry of metabolism.

What distinguishes the biochemistry of one individual from another and makes for different nutritional wants? The "recommended allowance" for thiamine, for example, is about 1.8 mg. per day, varying more or less according to sex, age, weight and activity. This allowance, like those for other nutrients, was set up to provide a margin of safety to include persons

whose needs might be greater than average. Thus, even among persons of the same sex, age and weight and muscular activity, 1.8 mg. of thiamine may be more than enough for some and just right for others. In a small percentage of cases, this amount may fall far short of satisfying the thiamine needs thereby resulting in vitamin deficiency. Such cases, for one reason or another, appear to have vitamin requirements even greater than those provided by the safety margin of the recommended allowances.

The reasons for differences in requirements are still not clearly understood. In general terms the explanation may lie in the efficiency of utilization of the various nutrients which is, in turn, under genetic control. Thus, it is well known that vitamins are significant in the body economy for the production of enzymes, which in turn regulate and control most of the vital processes of cellular metabolism. If one person can synthesize an enzyme more efficiently from a given supply of vitamins than another, that is, if the bottleneck in the synthesizing process lies in the concentration of the vitamin, then the two persons may differ in their quantitative vitamin requirements.

The concept that inherited differences in biochemical makeup may lead to differences in requirements of nutrients and thereby to disease if these requirements are not satisfied, is a new approach to the etiology and therapy of certain types of disease. If the individual with the hereditary trait is supplied with all that he needs of a nutrient — which may be far more than "average" requirements — the hereditary trait which otherwise would be damaging is offset or overcome. If, on the other hand, he consumes an "average" diet, he will have an inadequate supply of certain nutrients and the deficiency symptoms will become apparent.

This new concept of genetotrophic disease has been suggested and studied by R. J. Williams and his associates at the University of Texas. Following a preliminary investigative period the Williams group has made a bold attempt to deal with alcoholism as a typical manifestation of a genetotrophic disease on the basis of their belief that alcoholism is due in large part to hereditarily increased requirements of many of the common B vitamins.

In former times alcoholism was considered as a moral lapse, a sin or a crime and was treated accordingly. In more recent times, this concept, although still not completely forgotten, has been replaced to some extent by a psychological or psychotherapeutic approach. The Williams school, although recognizing the significance and importance of psychological influences and treatment, has attempted to show that alcoholism has a biological and biochemical basis and that therapy may be instituted accordingly. As A. J. Carlson says, "In my opinion, he (Williams) has opened a new and

important gate to the solution of one of the serious problems of mankind. Even if there are failures or partial failures, medical science and practice will be enriched and new ways may be opened for further advance. His ideas and recommendations should by all means be given adequate tests." If the working hypothesis of genetotrophic disease does lead, in fact, to a means of controlling alcoholism, the social and personal benefits will be immense.

## *Individual Metabolic Patterns:*

The key to the genetotrophic approach to disease lies in the recognition of the fact that *even among normal persons* there exist distinctive individual variations in metabolic patterns. The metabolic pattern, as described by Williams is a designation used to indicate the biochemistry of reactions occurring in any one particular individual. It refers to the nature and extent of the numerous biochemical reactions in the various tissues and organs of a given individual.

Studying and measuring the hundreds of complex, integrated chemical reactions that go on in an individual would, of course, be an impossible task. For this reason, the Texas group elected to study a limited number of metabolic reactions selected from the point of view of ease of observation and quantitative measurement. As they pointed out, their "patterns" are quite fragmentary and they do not necessarily include the most striking items or by any means the most important ones; they are simply items which show distinctiveness and which can be measured practically by objective means and without inconveniencing the subjects.

For these reasons, the metabolic patterns studied were limited to the following categories: (1) taste sensitivity, (2) salivary components, and (3) urinary components. Under these three categories, some thirty-one factors were measured. All, except the first five, by methods involving paper chromatography. (Table 1).

Findings for these thirty-one factors were plotted, for each individual examined, in a chart composed of polar coordinates. Figure 1 illustrates such a chart for a hypothetical individual all of whose measurements are considered to be average.

Figs. 2–13 represent corresponding charts for twelve actual individuals. It is to be noted that the hypothetical individual's chart bears no resemblance to that of any of the actual individuals and that, further, there is no such thing as a "normal" or "average" pattern. Each individual examined, whenever tested, apparently exhibits a characteristic pattern of measurements which is distinctive for that individual alone. While there are,

**TABLE I.**

**BIOCHEMICAL CHARACTERISTICS STUDIED**

*Taste Sensitivity to:*
1. creatinine
2. sucrose
3. potassium chloride
4. sodium chloride
5. hydrochloric acid

*Salivary Constituents:*
6. uric acid
7. glucose
8. leucine
9. valine
10. citrulline
11. alanine
12. lysine
13. taurine
14. glycine
15. serine
16. glutamic acid
17. aspartic acid

*Urinary Constituents:*
18. citrate
19. base RF 0.28, 0.20
20. acid RF 0.32
21. gonadotropin
22. pH
23. pigment/creatinine
24. chloride/creatinine
25. hippuric acid/creatinine
26. creatinine
27. taurine
28. glycine
29. serine
30. citrulline
31. alanine

in every case, day-to-day variations in saliva and urine compositions and in taste thresholds, certain items at least stand out as grossly distinctive and the patterns as a whole remain nearly constant. It is interesting to note the similarity between the patterns in Fig. 12 and Fig. 13 — a similarity which is not approached by any other two subjects. These two figures represent the metabolic patterns for two identical twins, and while the patterns are by no means identical, their similarity is an indication of the postulated genetic origin of biochemical behavior.

## *The Genetotrophic Concept of Disease:*

The highly individualized metabolic patterns of both animals and human beings are a reflection of individual genetic makeup. Williams and coworkers (1) have postulated that such genetic variations among "normal"

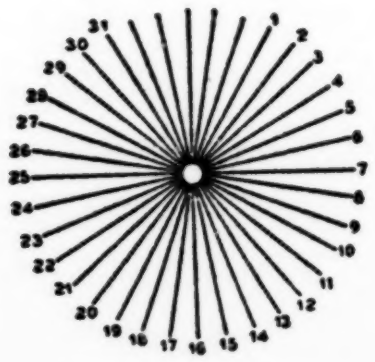


FIGURE 1

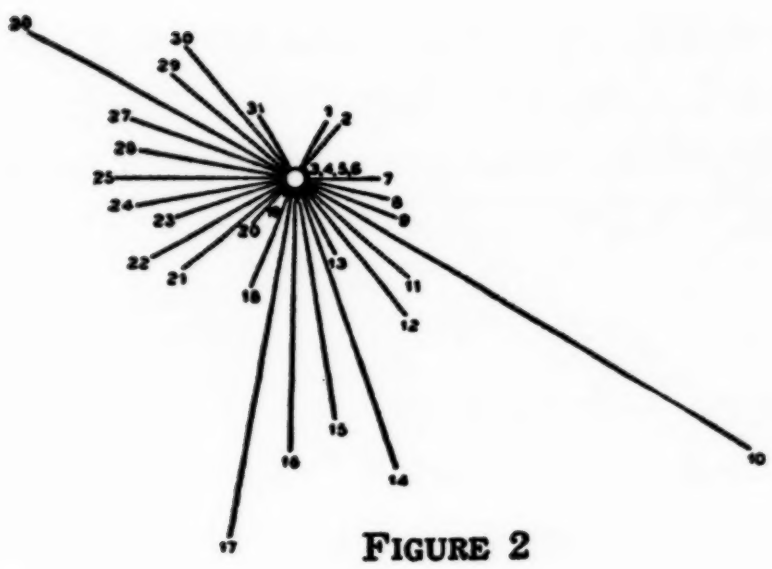

FIGURE 2

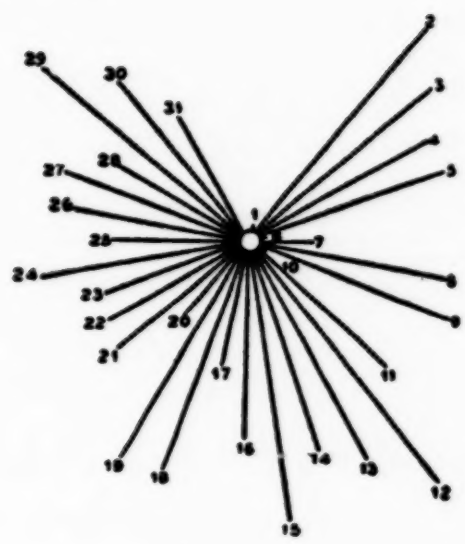

FIGURE 3

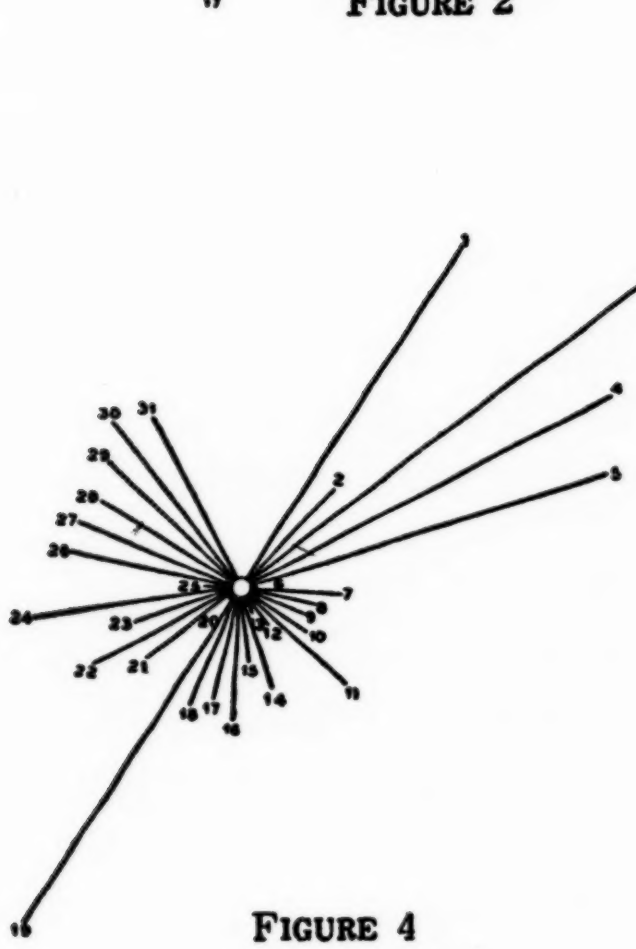

FIGURE 4

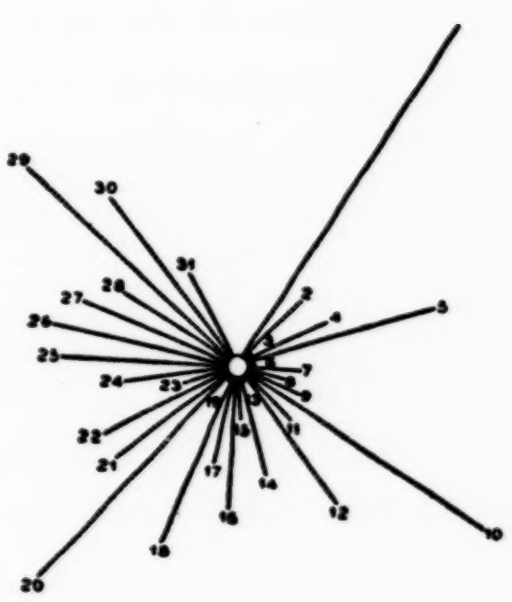

FIGURE 5

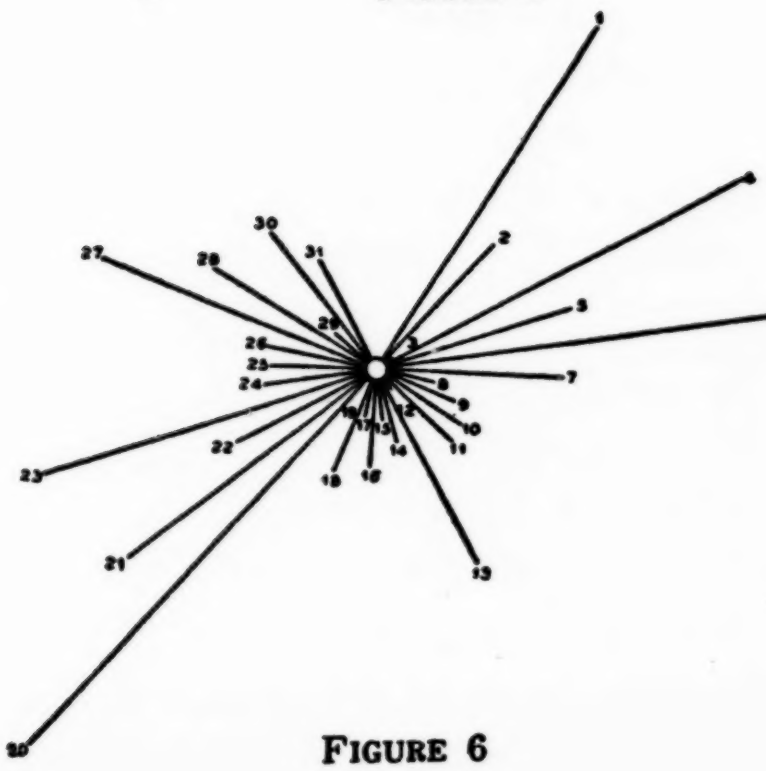

FIGURE 6

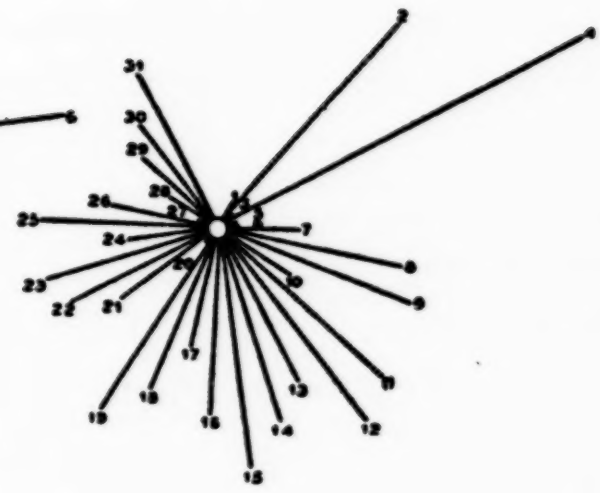

FIGURE 7

(FIGS. 1–13). Taste Sensitivity: 1. Creatinine, 2. Sucrose, 3. KCl, 4. NaCl, 5. HCl. Salivary Constituents: 6. Uric acid, 7. Glucose, 8. Leucine, 9. Valine, 10. Citrulline, 11. Alanine, 12. Lysine, 13. Taurine, 14. Glycine, 15. Serine, 16. Glutamic acid, 17. Aspartic acid. (contd. p. 34)

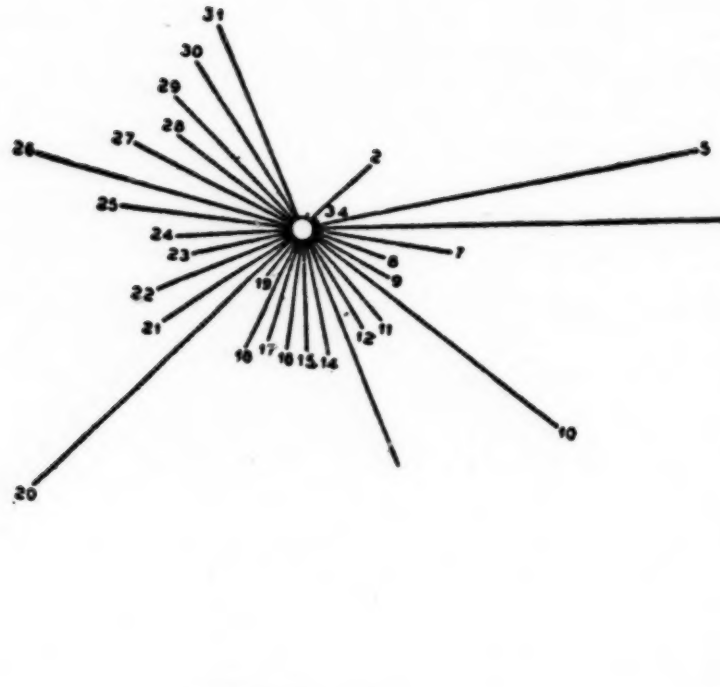


FIGURE 8

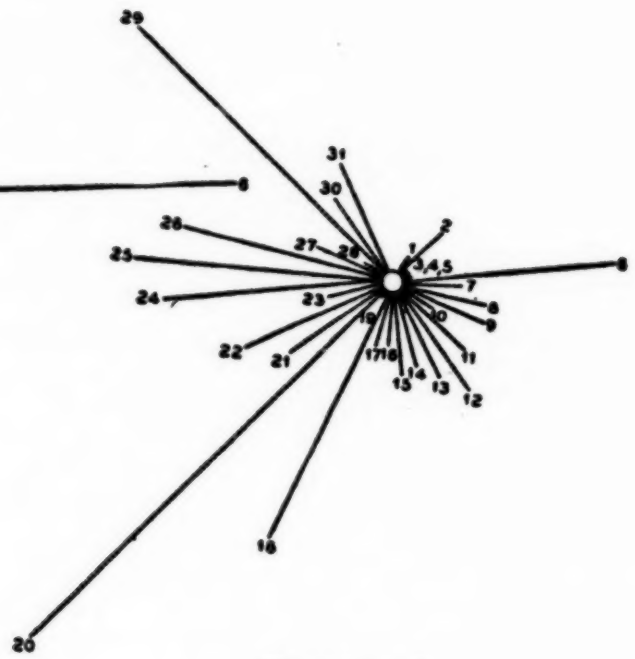


FIGURE 9

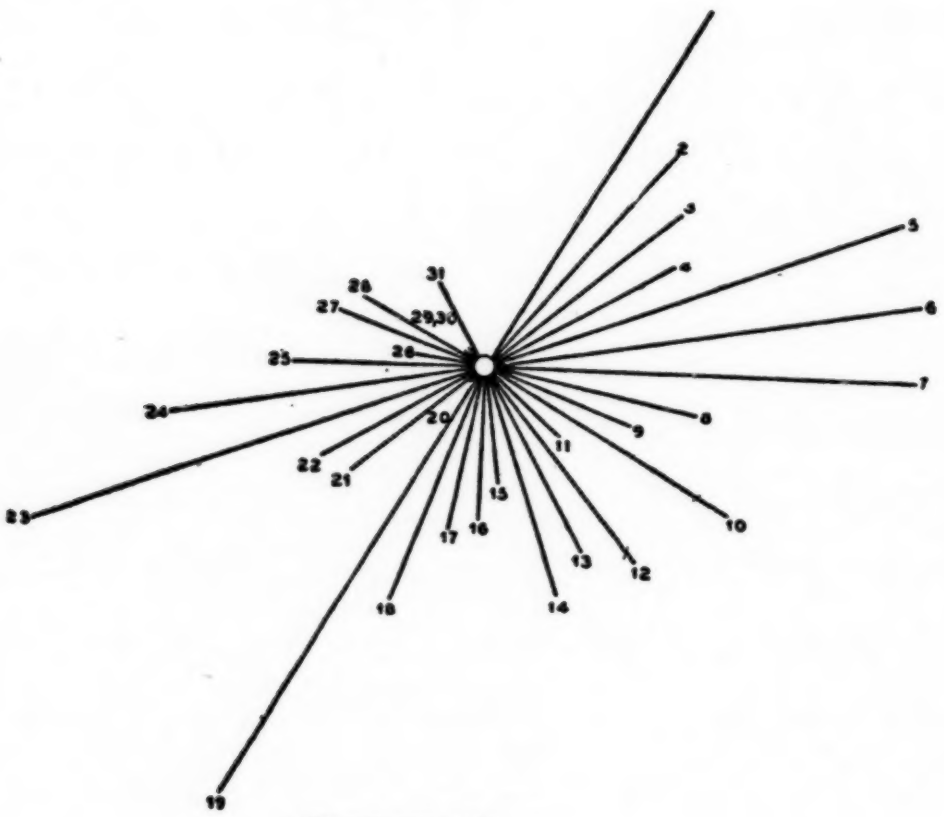


FIGURE 10

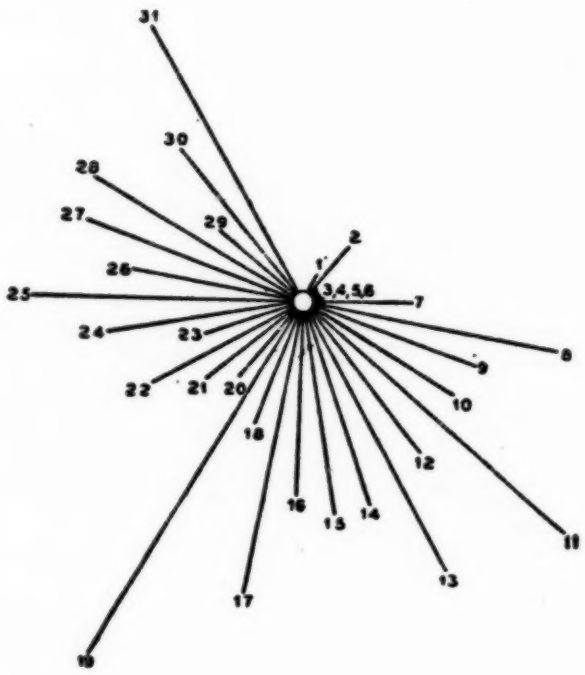


FIGURE 11

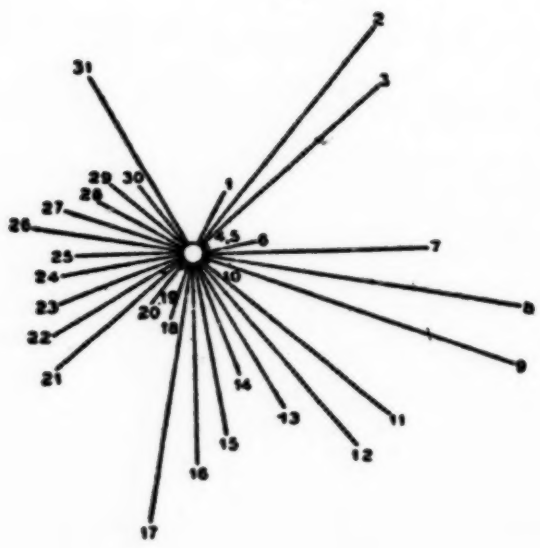


FIGURE 12

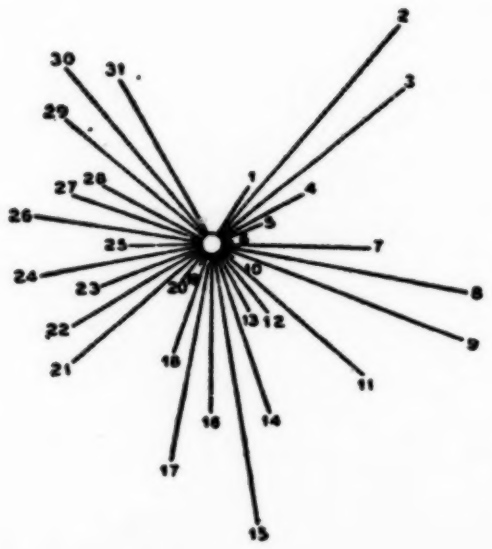


FIGURE 13

(FIGS. 1–13). (contd.) Urinary Constituents: 18. Citrate, 19. Base Rf.28, 20. Acid Rf.32, 21. Gonadotropin, 22. pH, 23. Pigment/creatinine, 24. Chloride/creatinine, 25. Hippuric acid/-creatinine, 26. Creatinine, 27. Taurine, 28. Glycine, 29. Serine, 30. Citrulline, 31. Alanine.

individuals may be reflected, for example, in variations in quantitative requirements for individual nutrients. When circumstances are such that genetic factors make necessary the supply of one or more nutrients in amounts appreciably higher than so-called "average" requirements, the result may be the development of a genetotrophic disease (i.e. *geneto,* of genetic or hereditary origin and *tropho,* pertaining to nutrition).

The combination of genetic factors with nutritional factors resulting in the development of disease represents, according to the group at Texas, a new concept as to the etiology of disease. Fundamental to this concept are recent findings in biochemical genetics (2)* particularly those studies which have led to the theory of partial genetic blocks (3, 4, 5). Such a block involves a heritable trait characterized by diminution — but not complete failure — of ability to carry out some specific enzyme-controlled biochemical reaction. Since a genetic defect of this kind may increase the need of the body for one or more nutritional factors†, the existence of such partial blocks in metabolism can explain why, for example, different species of animals require different types or amounts of nutrients, or why — in the same species — different individuals may vary in their quantitative needs for various nutrients.

On the basis of these findings Williams *et al* (1) have defined a genetotrophic disease as one in which the genetic pattern of the afflicted individual calls for an augmented supply of a particular nutrient (or nutrients) for which there develops, as a result, a nutritional deficiency even on a seemingly adequate diet. Partial genetic blocks, they suggest further, are probably commonplace in the inheritance of individuals and explain to a considerable degree why each person possesses a characteristic and distinctive metabolic pattern as revealed by the studies on taste discrimination and by urinary and salivary analysis. This concept offers also an explanation for the increasingly common finding that some people, even though partaking of apparently adequate diets — with respect to "average" requirements — nevertheless develop symptoms of vitamin deficiencies.

Genetically inherited patterns of metabolism, therefore, may increase certain nutritional requirements to the point where nutritional deficiencies may result, even on an adequate diet. Further, it is postulated on the basis of findings in the literature, such nutritional inadequacies may be manifested by marked changes in appetite — or even by cravings — for various types of foodstuffs. In some cases, the appetites appear to be homeostatic mechanisms which cause the individual to consume large amounts of a

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*The subject of biochemical genetics and its relation to nutrition and biochemistry will be reviewed in a subsequent issue of *Borden's Review of Nutrition Research.*

†Presumably because these may be needed to complete enzyme synthesis.

necessary nutrient to compensate for its deficiency or inefficient utilization in the body. Such cases include salt craving in adrenal insufficiency — whether induced by drugs, disease, pantothenic acid deficiency or adrenalectomy (6, 7, 8, 9); calcium hunger in parathyroid deficiency (10); aversion to phosphates in parathyroid deficiency (11); aversion to carbohydrate and protein and preference for fat in vitamin B complex-deficient experimental animals (12, 13).* In other cases, however, perverted appetites or cravings develop which bear no apparent compensatory relation to the existing deficiency, or may even be decidedly detrimental. (This subject has been more thoroughly reviewed in previous issues of this publication [14, 15]).

### *Alcoholism as a Genetotrophic Disease:*

The factors contributing to alcoholism are many and complex — psychological, emotional, cultural and the like — but the uncontrollable craving or appetite for alcohol which distinguishes the chronic alcoholic from other types of drinkers is believed to have an actual physiological basis and, therefore, to require physiological treatment. Williams and associates believe that this abnormal and uncontrollable craving for alcohol may be an example of a perverted appetite, such as previously described, resulting from nutritional deficiency. (Although there is no evidence to date, the possibility also exists that this phenomenon may also reflect a compensatory physiological mechanism, the nature of which is not yet understood).†

Evidence for the genetotrophic etiology of alcoholism comes from observations on variations in human behavior and susceptibility to alcohol; and from experimental studies on alcohol consumption as affected by dietary deficiency in both human subjects and animals.

**Animal Studies:** In a series of experiments with rats (16, 17, 18) it was found that *ad libitum* consumption of 10% ethyl alcohol (offered freely with water in separate cups, the positions of which were reversed daily to insure that each liquid was drunk by choice) varies widely among animals and may be profoundly influenced by diet.

For example, one group of rats on a stock diet consumed large amounts of alcohol rather consistently. Others avoided the alcohol at first but after a time drank increasing quantities. Still others drank spasmodically — heavily for a day or two, then not at all for a while, then heavily again. One rat consistently refused to drink the alcohol and chose only water;

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*Presumably to compensate for lack of these vitamins which are needed for proper metabolism of carbohydrate and protein.

†cf. page 37.

another drank very moderately, maintaining this same level of consumption over a prolonged period.

That these variations were due to inborn differences was strongly indicated by the fact that closely inbred strains were found to show similar drinking habits, whereas animals not closely inbred showed greater variations.

When animals from the original colonies were placed on diets lacking adequate amounts of various B vitamins, the differences in alcohol consumption tended to disappear. Within a short time, all of the animals began consuming alcohol at a fairly high level. Finally, when these animals were placed on abundant diets (superior to the stock diet in vitamin content) and again given a choice between water and 10 per cent alcohol, *none* of them drank appreciable quantities of alcohol.

Following these preliminary studies, further tests were made to determine which dietary factor or factors in the superior diet were responsible for the successful control of alcohol appetite. Not surprisingly, it was found that the factor — one or more of the B vitamins — varied for each animal. Findings similar to these were also reported by other laboratories (19, 20). In one case, the investigators have postulated the existence of an unknown principle, "Factor N," which they believe to be specifically involved in the control of appetite for alcohol (22).

Studies involving single vitamin deficiencies indicate that deficiencies of thiamine, riboflavin, pantothenic acid or pyridoxine are most likely to result in increased alcohol consumption by experimental animals and that treatment with these vitamins abolishes the excessive appetite for alcohol. Other vitamins such as vitamin A, choline and biotin, appear to have some effect also, but to a far lesser degree (21) (Table 2).

The effective vitamins appear to be those which function in the early stages of carbohydrate metabolism (riboflavin, thiamine and pantothenic acid) and in the utilization of amino acids as an energy source (pyridoxine)*.

Beerstecher *et al* (21) point out that rather than being a perverted appetite, the craving for alcohol may possibly be physiologic. They state:

> "It seems possible that the appetite for alcohol may arise as the result of its sparing action on some materials which are lacking in the body in adequate amounts. Further study of the exact modes of the metabolism of alcohol may show that as an energy source, alcohol spares the metabolic mechanisms needing

*The authors point out: "In early experiments in which animals were on diets deficient in B vitamins generally, the administration of these four vitamins did not 'cure' the rats whereas a more complete supplement did. It seems that to be free from alcohol appetite, rats must have their entire metabolic machinery functioning satisfactorily, but that certain deficiencies are more effective than others in promoting the appetite."

the above vitamins in a manner analogous to that in which it is known to spare thiamine-containing systems."

They add the further interesting observation that the four vitamins referred to above all have hydroxyl groups which are phosphorylated in the functional form of the vitamin. In this connection, they add that Verzar and coworkers have previously shown that the phosphorylation of riboflavin is under adrenocortical control, and that a similar situation may well hold for the conversion of the other vitamins in this group to the active coenzymes. Such a consideration may help explain the data obtained by other workers indicating an interrelationship of the adrenal cortex with alcoholism.

**TABLE II.**

***Tabulation of Composition of Single Vitamin Deficiency Diets***

| Component of Diet | | Vitamin Deficient from Diet | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Vitamin A (8) | Thiamine (9) | Riboflavin (10) | Pantothenic Acid (11) | Vitamin $B_6$ (12) | Choline (13) | Biotin (14) |
| Sucrose | % | --- | --- | --- | 68% | 68% | 68% | 73% |
| Cornstarch (Argo) | % | 65% | --- | 63% | --- | --- | — | — |
| Dextrinized rice starch | % | --- | 64% | --- | --- | --- | — | — |
| Casein* | % | 18% | 13% | 18% | 18% | 18% | 17.7%†† | 8% |
| Egg white† | % | --- | --- | --- | --- | --- | — | 10% |
| Crisco | % | --- | --- | 3% | 8% | 8% | — | — |
| Wesson oil | % | 5% | --- | --- | --- | --- | — | 5% |
| Lard | % | --- | --- | --- | --- | --- | 10% | — |
| Salts‡ | % | 4% | 3% | 4% | 4% | 4% | 4% | 4% |
| C.L.O.§ | % | --- | 1% | 2% | 2% | 2% | — | ‖ |
| Cystine | % | --- | --- | --- | --- | --- | 0.3% | — |
| Yeast¶ | % | 8% | 20%** | --- | --- | --- | — | — |
| Thiamine mg./100g. diet | | --- | --- | .20 | .20 | .20 | .20 | .20 |
| Riboflavin mg./100g. diet | | --- | --- | --- | .20 | .30 | .20 | .20 |
| Niacin mg./100g. diet | | --- | --- | 2.50 | --- | 2.50 | — | — |
| Choline mg./100g. diet | | --- | --- | 200. | --- | 200. | — | 100. |
| Calcium pantothenate mg./100g. diet | | --- | --- | 250. | --- | 250. | .20 | 1.00 |
| Pyridoxine mg./100g. diet | | --- | --- | .30 | .20 | --- | .20 | .20 |

*Borden's Labco Brand Vitamin Free.
†Palpable desiccated powdered egg white.
‡GBI Salt Mixture No. 2.
§Rexall, 2000 USP units Vitamin A and 200 USP units Vitamin D per gram.
‖Two drops Navitol with Viosterol per rat per week (3300 USP units Vitamin A, 660 units Vitamin D).
¶Anheuser-Busch, Primary Dried Yeast, Strain G.
**Autoclaved six hours.
††Extracted four times for two hours each time with boiling 95% ethanol.

Recent reports on the possible role of pantothenic acid as a catalyst in the synthesis of cortisone by the adrenal gland (22) add still another possible explanation for the apparent value of both this vitamin and cortical hormones in the therapy of alcoholism.

## *Clinical Studies:*

The results of animal studies clearly showed that although alcohol consumption is a highly individual matter, probably under genetic control, it can be induced in all animals by marginal diets and can then subsequently be "cured" nutritionally by eliminating the deficiencies. These findings prompted similar investigations with human subjects.

**Individual Variations:** In human beings, too, alcohol consumption varies widely. Furthermore, there exist tremendous differences among people in the physiologic response to alcohol.* It has been found, for example, that among 1,000 subjects, 10.5% were diagnosed as intoxicated when the alcohol concentration in the blood reached 0.05%; whereas a little over 6½% of the subjects were judged to be sober even though the alcohol concentration in their blood reached a level of 0.40% — eight times as high (23). Not only that, but at this same blood concentration of alcohol — commonly regarded as close to the lethal point — such wide variations exist among people, that one person may be judged entirely sober, while another may be so seriously affected as to be in coma.

Another cause for variation in response to alcohol is the rapidity with which alcohol disappears from the blood. Among a limited number of subjects, for example, it was found that one subject showed a rate of disappearance of 0.00176 mg. of alcohol per ml. of blood, whereas another showed a rate of disappearance of 0.00317 mg. per ml., even though the alcohol dose was larger in the latter.

Other variabilities include taste reactions, psychic reactions, physiologic tolerance and appetite for alcohol. In a group of young children aged 4–10 years, for example, it was found that most of the subjects disliked alcohol solutions in concentrations over 10–15 percent, but about 8 per cent of the children liked samples as strong as 50 percent alcohol (25). Among adults, acute effects of alcohol may include such diverse responses as drowsiness, belligerance, gaiety, mournfulness, irritability. Still others become ill on relatively small amounts of alcohol and are thus automatically protected from alcoholism by being unable to physically hold their liquor.

The most significant variation among individuals insofar as the development of alcoholism is concerned is the phenomenon of a persistent craving for alcohol exhibited by certain individuals. It is well known, for example, that some individuals can drink moderately — or even immoderately — for a long period without developing the intense and persistent craving which marks the typical alcoholic. An interesting example is cited in the case of

*Such differences in response are also well exemplified by widely varying individual reactions to drugs, stimulants and the like.

a man who lived to the age of 93, having drunk close to a quart of Scotch whiskey every day for the last 60 years of his life, all the while competently managing an important business (26). On the other hand, there are young persons who early in life develop an uncontrollable appetite for alcohol and who, as a result, become unable to live normal lives.

All of these variations and individual peculiarities are believed by Williams to be a reflection of inherited metabolic patterns (27). Without discounting the effects of environment, ethnic or cultural influences, or psychological motivation (stress, escapism, etc.) or the need for psychological aid and rehabilitation in addition to other therapy, Williams states:

> "If our hypothesis is correct . . . no psychological *(or other)* stresses can make an individual an alcoholic unless he has inherited a metabolic pattern which renders him susceptible."

As Kraines (28) has also pointed out in this connection:

> "If one reviews many cases of psychoneuroses, psychoses . . . alcoholism . . . one is struck by the fact that the psychologic and environmental forces which preceded most of these illnesses are as a group essentially the same regardless of the type of illness. Even more impressive is the fact that many persons who remain 'normal' may be subject to stress of the same character and intensity as are those who break down with some form of psychiatric illness."

**Biochemical Studies:** Preliminary studies, on a very small scale, have been begun in an attempt to explore various metabolic traits of alcoholic and non-alcoholic individuals in order to discover whether any detectable differences do exist between these two classes. Basic to this study have been detailed, fairly long term studies of the metabolic patterns of normal individuals based on paper chromatographic analysis of urine, blood and saliva and on taste sensitivity reactions (29).

With this information as a guide, a study was undertaken with twelve subjects — eight controls and four compulsive drinkers (members of Alcoholics Anonymous, studied during non-drinking periods).

Approximately 60 metabolic items were studied. The findings for the alcoholic group are collectively summarized in Table III.

It can be noted from this table that 11 metabolic items have been found for which the probability of the observed difference between alcoholics and nonalcoholics being accidental is from 1% to 10%. For nine additional items the corresponding probabilities are 10–20%. These data strongly suggest that compulsive drinkers do have common metabolic characteristics.

An examination of those items associated with mineral balance indicates that while serum and urinary sodium are not significantly different in the alcoholic group, salivary sodium is appreciably higher, suggesting somewhat decreased powers of sodium retention. The potassium balance is ap-

## TABLE III (33)

### *Tabulation of High and Low Characteristics in Alcoholics in Order of Decreasing Significance*

(Numbers in parentheses are *P* values for difference between alcoholics and controls)
(S = saliva, U = urine, B = blood serum, T = taste threshold,
P = phagocytic index)

| High | Low |
|---|---|
| Sodium (S) (99) | |
| Hippuric acid (U) (99) | Gonadotropin (U) (96) |
| Uric acid (U) (95) | Citrulline(U) (95) |
| Uric acid (S) (95) | |
| Thiamine (U) (94) | |
| Citrate (U) (92) | |
| Magnesium (B) (92) | |
| Pigment/creatinine (U) (91) | Phosphorus (B) (90) |
| Weak acids (U) (88) | Taurine (U) (88) |
| Sodium chloride (T) (88) | *Bacillus subtilis* (P) (88) |
| pH (U) (87) | |
| Sulfate (U) (84) | |
| Lactate (U) (82) | Total amino acids (U) (82) |
| Glucose (S) (80) | |
| Pantothenic acid (U) (78) | Creatinine (U) (78) |
| Chloride (U) (77) | |
| Urea (U) (73) | Iron (B) (75) |
| KCl (T) (72) | |
| Sodium (B) (72) | |
| Sodium (U) (70) | |
| Taurine (S) (68) | |
| Lysine (S) (60) | Sp. Gr. (U) (60) |
| Alanine (S) (56) | Calcium (B) (58) |
| Glutamic acid (U) (56) | *Micrococcus* (P) (56) |
| Leucine (S) (54) | Pigment (U) (55) |
| Copper (B) (53) | |
| Potassium (S) (51) | |
| Carbon (P) (48) | |
| Volume (U) (46) | Sucrose (T) (44) |
| Alanine (U) (43) | |
| HCl (T) (43) | Creatinine (T) (42) |
| Glycine (S) (42) | Other amino acids (U) (42) |
| Phosphate (U) (38) | Glutamic acid (S) (38) |
| Potassium (B) (32) | Serine (U) (36) |
| | Aluminum (B) (28) |
| | Weak bases (U) (24) |
| | Citrulline (S) (22) |
| Serine (S) (20) | Glycine (U) (20) |
| γ-Aminobutyric acid (S) (15) | |
| Glucose (U) (14) | |
| Valine (S) (9) | |
| Aspartic acid (S) (0) | Aspartic acid (S) (0) |

*N.B.* The value of P is an indication of the probability in each case than an accidental effect would give a smaller difference from that observed; thus P values of .95 or greater mean that fortuitous differences would be as large as those observed only once in 20 or more times.

parently unchanged. Serum magnesium is apparently elevated and phosphate depressed, although the importance of these observations is questionable. Of some interest in this regard is the apparent elevation of taste threshold for sodium chloride (and perhaps potassium chloride), since it has been established that adrenally decortate animals have increased taste sensitivity for sodium (9). The fact that the urinary gonadotropin titer in alcoholics is significantly low is a point of considerable interest in itself, since many of the physiological properties of cortical steroids are shared by androgens (31). The observed increase in excretion of urea and depressed citrulline excretion fall well in line with the reported metabolic effects of androgen and cortical steroid deficiency. By contrast, however, the elevated uric acid excretion is contrary to the known effects of deficiencies in either gland. In connection with the studies on phagocytic indices, it is interesting that phagocytic activity has been found to be depressed in adrenalectomized rats and that administration of cortical extracts restored the activity (32).

In summary, the items that appear to be associated with alcoholism are:

*In saliva:* increased sodium and uric acid.

*In urine:* increased hippuric acid, uric acid, citric acid, unidentified weak acids, vitamin $B_1$, pigment; increased pH (acidity)
decreased gonadotropin (hormone), taurine and citrulline.

*In blood:* increased magnesium
decreased phosphorus

*Taste:* increased taste sensitivity to salt.

**Significance of Studies:** There are at least two questions which naturally arise in a study of this type: (1) does diet have an appreciable effect on the all-over metabolic pattern? and (2) is the metabolic pattern truly a predisposing cause of alcoholism, or rather, does alcoholism cause an abnormal deviation in the metabolic pattern? Clear cut answers to these questions necessarily require a great deal of further research, but Williams *et al* believe the evidence at present is such as to indicate that individual metabolic patterns are genetically determined, are insignificantly altered by diet, and constitute a predisposition to alcoholism rather than vice versa. This evidence includes results of actual diet studies (a shift from self-selected diets to uniform U. S. Army K rations; studies of infants on diets consisting almost entirely of milk; etc.) which show that distinctive patterns exist whether people are on self-selected diets or on identical diets and that the patterns remain essentially the same even when diets are drastically changed. With respect to the latter question, Williams (32) states:

"It seems to us very unlikely that excessive drinking would cause a change in pattern which would remain changed for many months after the drinking ceased. The whole background of information on metabolic patterns which we possess fits in well with the hypothesis that the tendency toward excessive alcohol consumption has as a forerunner the possession of a characteristic metabolic pattern."

## *Nutritional Therapy of Alcoholism:*

The successful induction and control of alcohol appetite in experimental animals by nutritional means naturally suggested a trial of the same procedure to control alcohol appetite in human subjects. Added to this were the results of metabolic studies in man which strongly indicated that the biochemistry of alcoholic individuals deviates significantly in at least several characteristic aspects from that of the non-alcoholic individual and that, therefore, alcoholism may be amenable to nutritional therapy in line with the principles of the genetotrophic concept.

Because it is exceedingly difficult to determine for each individual concerned, the exact nature and extent of his inherited nutritional requirements, nutritional therapy of a "shotgun" type was instituted. That is, a wide variety of nutritional factors, in amounts well over the generally accepted "average" requirements, was administered. Fortunately, this is made possible by the fact that overloading with nutrients — at least to the extent practiced in these treatments — is not likely to do any harm and in this way, each individual has an opportunity to receive the increased amount of the particular elements of which he requires more (along with a harmless excess of others which he may not need). It is quite possible that the day will come when scientific exploration along the lines of biochemical individuality will have advanced to the point where physicians will be able to test patients to determine their specific needs and to prescribe accordingly, but at present, treatment and study are necessarily limited to multi-nutrient therapy.

The number of alcoholics treated by nutritional means thus far have been relatively few. This includes persons treated not only by Williams' group, but by physicians throughout various parts of the country. To date, the results of these studies have not yet appeared in the literature, but they have been briefly described by Williams (30) from experiences at Texas and from reports made to him by other participants in this experiment.

Basic to the procedure is the establishment of good eating habits and the provision of a well-balanced diet providing generous amounts of high quality protein (meat, milk, fish, eggs, cheese), and other nutritional essentials following the "basic seven" food group pattern:

1. milk and other dairy products
2. meat, poultry, fish and eggs
3. oranges, tomatoes, raw greens or other vitamin C sources
4. green and yellow vegetables
5. potatoes and other vegetables and fruits
6. enriched or whole grain bread, flour, cereals
7. butter and fortified margarine

Because there is a need for a superabundance of one or more of the food essentials and because diet alone cannot be relied upon to provide the necessary amounts of these, the basic diet is supplemented with therapeutic capsules of the following composition:

**NUTRIENT CONTENT OF ONE CAPSULE**

| | | |
|---|---|---|
| Thiamine | 3.3 | mg. |
| Riboflavin | 2.67 | mg. |
| Nicotinamide | 10.0 | mg. |
| Calcium pantothenate | 10.0 | mg. |
| Pyridoxin | 3.3 | mg. |
| Biotin | 0.05 | mg. |
| Folic acid | 1.1 | mg. |
| p-Aminobenzoic acid | 11.0 | mg. |
| Inositol | 53.0 | mg. |
| Choline | 53.0 | mg. |
| Vitamin $B_{12}$ | 5.0 | mcgm. |
| Vitamin A | 6,667 | I.U. |
| Vitamin C | 33.3 | mg. |
| a-Tocopherol | 6.67 | mg. |
| Viosterol | 333 | I.U. |

The subject is started on a minimum of three capsules of the above composition daily and the amount gradually increased, provided there is no intolerance, to a total of nine capsules daily, taken with meals. Depending upon the individual response, the number of capsules may have to be continued at nine per day or may be reduced to from 2 to 6 per day. In all cases, however, because of the inherited need for increased intake of certain of these nutrients, the use of these therapeutic supplements must be continued throughout the life of the individual, just as, for example, a diabetic person requires insulin throughout his life in order to function properly.

The following case history described by Williams (33) illustrates the type of response which has been obtained in many of the cases treated:

"The first patient to undergo our treatement was a man in his middle forties who had been an alcoholic for ten years and a heavy drinker for twenty. He had tried to get help from psychiatry and from Alcoholics Anonymous without success, had been forced out of his home, and was

desperate when I first interviewed him. His craving for alcohol was accompanied by such definite symptoms that he assured me that he could tell without the slightest doubt if his craving were abolished or materially abated.

"He was given no sales talk about what could be done for him (we didn't know) and no suggestion as to what changes he might conceivably expect. He took the treatment and reported back to us periodically any changes *he* observed. In one month he reported that he could now go to bed earlier and sleep better and he could tolerate coffee without previously having had an alcoholic drink (which he could not do before). The improvement in sleeping we regarded as a favorable sign (though we had not anticipated it) because alcoholics frequently suffer from insomnia and the boredom of wakefulness contributes to their desire for drink. About this time he began to feel sure that he was being benefited.

"After four months of abstinence accompanying the treatment, he came to us, told us he *knew* the compulsion was gone, and that he intended to demonstrate it by going to a beer parlor, drinking several bottles of beer, and returning to us sober. Beer was his favorite drink, but one bottle — always followed by another — had been enough in the past to send him off on a long and devastating spree.

"We regarded his experiment as dangerous — we had thought total abstinence the best goal for an alcoholic — but he insisted that he knew what he was doing and that the compulsion was gone. So he carried out the experiment, after telling us in advance when it was to be performed, and came back to us the next day perfectly sober, ready to relate his experience. He said that after the first two or three bottles he deliberately forced himself to drink more—he did not crave or desire more, but wanted to put himself to a severe trial. Having passed this initial test with such marked success, he continued to drink two or three bottles of beer daily, overjoyed that he could drink as he had always wanted to—moderately.

"This continued for three months' time; he began to be sure of himself, and when he ran out of the capsules we were furnishing, he did not ask for more. He regretted it later, however, when the compulsion returned and he went on a spree. After this episode, he applied for more treatment, which again abolished his compulsion, and he continued to drink beer moderately as before. At Christmastime a former drinking associate came to town and he with his companion *deliberately* got drunk. He assured me that there was no compulsion whatever about it, that it lasted only a day, and that it bore no resemblance to one of his typical experiences of the past. After a period of many months since he began the treatment, he is still drinking beer moderately and has lost his compulsion.

"This individual probably constitutes the first case on record in which an alcoholic has become a moderate drinker."

## *Conclusion:*

No claim has been advanced by Williams that the genetotrophic approach to the cure of alcoholism is a completely successful one, nor is the importance of psychological approaches to the problem in any way minimized. It is to be recognized at the present incomplete level of information concerning metabolic and nutritional requirements, that the nutritional supplements given may, in some cases, be inadequate. Furthermore, it is well recognized today that an intimate relationship exists between mental and emotional disturbances and physical ones. Psychosomatic approaches to therapy recognize that body functions can be markedly upset by such influences. It is possible, indeed, that emotional and mental disturbances may cause heightened nutritional requirements, as well as vice versa. It has been increasingly recognized in the last decade or so, that alcoholics are frequently undernourished and nutritional therapy of advanced alcoholic conditions such as delirium tremens, alcoholic cirrhosis,Wernicke's syndrome, Korsakoff syndrome, etc. is frequently effective (34, 35). The contribution of the genetotrophic concept is that body deficiencies resulting from hereditary factors may give rise not only to the severe neurological complications of alcoholism, but to the development of alcoholism itself.

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